Clarithromycine-Induced Ventricular Tachycardia in a Geriatric Patient Using Multiple Drugs

Çoklu İlaç Kullanımı Olan Geriatrik Hastada Klaritromisin'e Bağlı Ventriküler Taşikardi

Clarithromycine-Induced Ventricular Tachycardia

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Özet

Uzun QT sendromu ani kardiak ölüme neden olabilen idiyopatik, iyatrojenik veya konjenital sebeplerle gözlenebilen bir kardiyak repolarizasyon bozukluğudur. İyatrojenik form daha çok ilaçlara ve elektrolit dengesizliğine bağlıdır. QT aralığı uzaması sıklıkla antiaritmik ilaçlara bağlı olarak görülse de antibiyotikler ve antiepileptikler ile de karşımıza çıkabilir. Yaşlılardaki olumsuz ilaç etkileşimleri; çeşitli klinikopatolojik formlarda karşımıza çıkabilir. Bu gibi durumlarda tedavide; ilave ilaç uygulamasından önce, kullanılan ilaçların yan etki potansiyellerinin göz önüne alınması gerekmektedir. Çalışmamızda; atipik pnömoni sebebiyle yoğun bakımımızda Klaritromisin tedavisi başlanan; komorbiditeleri sebebiyle çoklu ilaç kullanımı olan 91 yaşındaki trakeostomili erkek hastada tedavinin 3. gününde gözlenen QT uzaması ile ventriküler aritmi gelişimini ve sonrasındaki tedavi yaklaşımını sunmayı amaçladık.

Anahtar Kelimeler

Klaritromisin; Uzun QT Sendromu; İlaç Yan Etkisi

Abstract

Long QT syndrome is a cardiac repolarization disorder, which can be either idiopathic or congenital, and cause sudden cardiac death. The iatrogenic form is generally associated with drugs or electrolyte imbalance. Although prolonged QT interval is frequently seen due to antiarrhythmic agents, it can also be seen with antibiotics or anti-epileptics. Adverse drug interaction can manifest in several clinicopathological forms in elder individuals. In such cases, potential adverse effects of drugs used should be taken into consideration before prescribing additional drugs. Here, we present a case of clarithromycine-induced ventricular arrhythmia accompanied by QT prolongation on the third day of therapy, and the subsequent therapeutic approach, in a 91-year-old man. The patient was taking multiple drugs due to comorbid conditions and was prescribed clarithromycine therapy in the intensive care unit.

Keywords

Clarithromycine; Long QT Syndrome; Adverse Drug Interaction

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Introduction

Adverse effects due to polypharmacy can be observed in elder individuals. Thus, potential adverse effects of drugs used should be taken into consideration before prescribing additional drugs in such cases.

Long QT syndrome (LQTS) is a cardiac repolarization disorder, which can be either idiopathic or congenital, and cause sudden cardiac death. LQTS is important because it can cause severe polymorphic ventricular tachycardia [torsade(s) de pointes]. Many cardiac and non-cardiac drugs can cause torsade(s) de pointes by prolonging the QT interval [1].

Clarithromycine, a macrolide antibiotic, reaches steady-state serum concentration within 3 or 4 days. It is often preferred as first-line therapy in community-acquired pneumonia. Adverse effects including acute coronary syndrome, decompensated heart failure, sudden cardiac death, and severe arrhythmia have been reported [2].

Here, we document the development of ventricular arrhythmia with QT prolongation on the third day of clarithromycine therapy, and the subsequent therapeutic approach, in a 91-year-old man with multi-drug use for chronic obstructive pulmonary disease (COPD), atrial fibrillation (AF), congestive heart failure (CHF), and Alzheimer's in whom clarithromycine was prescribed for atypical pneumonia in the intensive care unit (ICU).

Case Report

A 91-year-old man with a history of CHF, COPD, AF, and Alzheimer's disease presented to the emergency department with dyspnea. He was diagnosed with community-acquired pneumonia and admitted to the ICU.

On the anamnesis, it was found out that the patient was using diltiazem, coumadin, aldactone, formoterol, and donepezil. In physical examination, vital signs were as follows: heart rate, 122/minute; blood pressure, 91/45 mmHg; respiratory rate, 19/min; and SpO2, 98%. AF and crackles at middle-lower pulmonary zones at the right were detected. The patient was prescribed ampicillin-sulbactam (4x 1 g; IV) and clarithromycine (2x500 mg; IV).

Polymorphic ventricular tachycardia (Picture 1) with prolonged QT interval (QTc: 464 ms) developed after the fifth dose of clarithromycine and elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), gamma-glutamyl transferase (GGT), bilirubin total (T Bil), and bilirubin direct (D Bil) levels (Table 1) were detected on blood tests on the second day after admission. Serum potassium (K) levels were within normal limits. Thus, the drugs used and their potential interactions were questioned. Clarithromycine was implicated as a cause of arrhythmia. Thus, clarithromycine was withdrawn.

Picture 1. Polymorphic ventricular tachycardia

Tablo 1. Laboratory data of the patient

Test*	Day 0	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
AST	35	901	566	304	159	92	59	52	39
ALT	25	896	629	481	347	257	199	156	118
GGT			173	175		163			136
ALP			153						
LDH			505	339		367			340
T Bil			2	2					1
D Bil			0,9	0,9		1			0,8
K	4,2	4,1	4,2	4	3,9	4,2	4	3,9	4,4

* AST : aspartate aminotransferase ALT: alanine aminotransferase GGT: gamma-glutamyl transferase ALP: alkaline phosphatase LDH: lactate dehydrogenase, T Bil: bilirubin total, D Bil: bilirubin direct, K: potassium

The patient was discharged on the 14th day of ICU admission.

Discussion

The increase in chronic diseases due to advancing age leads to polypharmacy, which is defined as an increased number and frequency of drug use in patients. In addition, alterations in drug metabolism and elimination increase risk for adverse drug interaction.

In the elderly population, the drugs frequently causing adverse depressant effects on the CNS are antibiotics, analgesics, anticoagulants, antihypertensive agents, bronchodilators, diuretics, and oral hypoglycemic agents. Suggestive findings include confusion, irritability, arrhythmia, memory loss, extra-pyramidal findings (Parkinsonism, delayed dyskinesia), constipation, and incontinence [3].

In a study conducted on 3695 patients in the United Kingdom, it was found that drug adverse effects accounted for 14.7% of hospitalizations with a markedly longer hospital stay [4]. In a study of 335 patients aged ≥65 years who were using 9 or more drugs, it was found that adverse effects were present in 207 drugs and that adverse effects were increased by 2.33 fold in patients using ≥9 drugs when compared to those using <9 drugs [3].

The lowest possible drug doses should be prescribed and drugs with potential adverse effects should be used for shorter periods, particularly in elderly patients. In such patients, accurate dose adjustment and monitoring of clinicopathological changes are essential. A recommended solution is to treat adverse effects by simplifying the drug regimen rather than adding new drugs.

LQTS is characterized by prolonged QT interval, tachyarrhyth-

mia, syncope, and sudden cardiac death. It limits itself, but occasionally it can progress to ventricular fibrillation. If the abovementioned symptoms are present, drug-related LQTS should be preferentially considered as the cause in patients receiving a drug known to lead to prolonged QT interval [1].

Heart rate should be taken into consideration to confirm abnormal prolongation in QT interval because QT is prolonged in cases of bradycardia whereas it is shortened in cases of tachycardia. In the diagnosis of LQTS, corrected QT interval must be calculated by using Bazett formula [QTcB (Heart rate-corrected QT interval) = QT Interval / √RR (Interval from the onset of one QRS complex to the onset of the next QRS complex)]. The upper limit for QTc is 0.44 seconds [5].

In our case, ampicillin-sulbactam, clarithromycine, low-molecular weight heparin, and a gastro-protective agent were added to the current drugs. The patient was closely monitored for potential complications and QT interval was calculated as 474 msn on ECG obtained after onset of arrhythmia. Clarithromycine, which was implicated for arrhythmia, was withdrawn.

Erythromycin-related LQTS are frequently observed; however, clarithromycine-related LQTS has been reported less commonly in the literature. Clarithromycine, known to cause QT prolongation, is a macrolide antibiotic. It can also cause ventricular arrhythmia and elevated liver enzymes [2].

Syncope and abnormal ECG findings are two major symptoms of LQTS. In general, clinical findings are corrected by the withdrawal of drug; however, interventions including antiarrhythmic drugs, cardioversion, and pacemaker have been reported in the management of LQTS in the literature [6].

In patients with LQTS, torsade(s) de pointes may persist despite withdrawal of the drug. Salinas et al. [7] reported a patient admitted to ICU due to syncope and loss of consciousness on the 48th hour after initiation of ciprofloxacin with diagnosis of cholangitis. On ECG, tachycardia involving polymorphic QRS was detected and QTc was calculated as 596 ms. As a result, a temporary pacemaker was implemented in addition to withdrawal of ciprofloxacin. No novel clinical or electrocardiographic finding was observed; however, torsade(s) de pointes persisted in this patient.

Alesso et al. [8] initiated amiodarone infusion for AF with RVR and clarithromycine plus ciprofloxacin (due to penicillin allergy) in a 71-year-old patient with community-acquired pneumonia. The ventricle rate was decreased below 100 during follow-up; however, AF with RVR relapsed on day 3 and QT prolongation was detected by ECG on day 4. Mechanical ventilation was started in the patient with worsening clinical findings. Ciprofloxacin and clarithromycine were replaced by ceftriaxone; however, QT prolongation persisted beyond 48 hours after the withdrawal of drugs.

Buchanan et al. [9] reported a case with hypertension and fluoxetine use for depression in which clarithromycine was given for acute upper respiratory tract infection. Cardiac examination was performed due to two syncope attacks that developed within 2 days after prescription of clarithromycine. Serum K level was found to be at the lower limit of the normal range and torsade(s) de pointes was detected on ECG. As torsade(s) de pointes progressed to ventricular fibrillation, defibrillation was performed but the patient could not survive. Authors suggested female gender, hypokalemia, acute infection, and fluoxetine use as risk factors for poor prognosis.

Conclusion

QT prolongation is a severe clinical entity that can sometimes result in mild consequences and can be corrected by withdrawal of drug. However, it can have severe consequences requiring invasive interventions such as defibrillation or pacemaker implementation. In our case, withdrawal of the drug alone was sufficient for recovery due to lack of electrolyte imbalance, early recognition of arrhythmia, and the patient's mild clinical conditions not requiring cardioversion or pacemaker implementation. Normal sinus rhythm was restored after 12 hours.

When prolonged QT interval, ventricular tachycardia, and altered laboratory findings were observed in a patient as in our case, before adding a new agent (antiarrhythmic) for treatment, it should be considered that symptoms may be iatrogenic. Drugs in the patient's medical history should be reviewed, and suspected drugs should be withdrawn with close hemodynamic monitoring.

Competing interests

The authors declare that they have no competing interests.

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